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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,659	05/26/2006	Andrea Pastorello	50294/018001	5027
21559	7590	03/27/2008	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			KOSAR, AARON J	
			ART UNIT	PAPER NUMBER
			1651	
			NOTIFICATION DATE	DELIVERY MODE
			03/27/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No. 10/580,659	Applicant(s) PASTORELLO ET AL.	
	Examiner Aaron J. Kosar	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17, 19-61, 63 and 75-82 is/are pending in the application.
- 4a) Of the above claim(s) 2, 7-13, 15, 25-31, 35, 36, 38, 40, 41 and 43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61 and 63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/26/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on December 17, 2007 is acknowledged. The traversal is on the ground(s) that the intended use of the composition is different than that argued in the election/restriction requirement and that claimed composition is novel and unobvious over the art of Pavesio. This is not found persuasive for the reasons of record and because Applicant has argued limitations narrower in scope than the breadth of the claimed invention and limitations not required by the claimed invention; thus, the limitations that Applicant has argued argue an alternate combination than presented in the election/restriction requirement and/or are not required by the claims.

Applicant's election of the species is also acknowledged (see Remarks, page 2) as follows: (1) a benzyl ester of hyaluronic acid; (2) a biocompatible and biodegradable ceramic including (2)(a) a tribasic calcium phosphate; (3) hyaluronic acid benzyl ester with a percentage of esterification of between 55 and 100%; and (4) an osteoinductive factor.

Claims 1-17, 19-61, 63 and 75-82 are pending. Claims 18, 62, and 64-74 are cancelled. Claims 54-60, and 75-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 2, 7-13, 15, 25-31, 35, 36, 38, 40, 41, and 43, though further limiting of the generic invention, are drawn to species, including derivatives (B) through (F) and non-tribasic calcium phosphate/non-hydroxyapatite components. Claims 2, 7-13, 15, 25-31, 35, 36, 38, 40, 41, and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected species, there being no allowable generic or linking claim.

Art Unit: 1651

Applicant timely traversed the restriction (election) requirement in the reply filed on December 17, 2007. **Claims 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61, and 63** are pending and have been examined on their merits to the extent the claims read on the elected species.

The election/restriction requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 26, 2006 has been considered by the examiner. The citations to the International Preliminary Examination Report (IPER) and International Search Report (ISR) have been lined through on the IDS since the reports are part of the international stage of the instant Application, now entered into the national stage.

The documents have been placed in the Application file and the references listed in the IPER and/or ISR have been considered to the extent that the references have been individually listed in the IDS submitted on May 26, 2006 or have been cited by the Examiner and placed on a PTO-892. The references cited in the Search Report which are not provided individually on an IDS or cited on a PTO-892 have been considered, but will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references which are not presently of record on an IDS or PTO-892, printed on such resulting patent, a separate listing, preferably on a PTO/SB08A and 08B form, must be filed within ONE MONTH of the mailing date of this communication. NO EXTENSION OF TIME WILL BE GRANTED UNDER EITHER 37 CFR 1.136(a) OR (b) to comply with this requirement.

Specification

The disclosure is objected to because of the following informalities:

The specification appears to recite literal translations and untranslated words/phrases from the foreign priority document, for example the phrase "aventi uguali dimensioni" (page 18, line23).

The use of the trademarks including species of HYAFF[®] 11 and ACP[®], have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. To the extent that a tradename is used, it should: (i) be capitalized and include the appropriate trademark symbol wherever it appears (*e.g* ACP[®]) and to the extent supported by the original disclosure (ii) be accompanied by the generic terminology in the first recitation of the trademark in the specification and as necessary thereafter to clearly and unambiguously identify the trademarked composition. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks (see MPEP 608.01(v)).

Appropriate correction is required.

Claim Objections

Claims 33 and 42 are objected to because of the following informalities:

The separation of claims by indentation of the elements, appears to be bulleted and/or omitting an alphanumeric label of each indentation. Whereas the alphanumeric label is not

Art Unit: 1651

required, the bulleting of indented material in the claims may potentially affect formatting at the time of printing, and thus the labeled or the labeling-free/bulleting-free indent is preferred.

Additionally, where a complex indent or series of indents comprising alternatives with subalterantives listed therein, the major separations should be grouped by separating with a ";" (e.g. in claim 33, "bone granules..origin; or..ceramics; or, ..") and the subgroups with the groups further separated by either further indents and/or a "," so as to avoid any potential confusion as to the interrelationships among the groups, subgroups, and combinations therein.

In claim 42, the term "to fixable to the layers" appears to be a literal translation of the foreign document or typographical error thereof.

Appropriate correction is required.

Double Patenting

Applicant is advised that should **claims 3-6** be found allowable, **claims 21-24** will be objected to under 37 CFR 1.75 as being a substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The claims are generally drawn to a multilayer composite material comprising a multicomponent inner matrix composite material and further comprising an association with at least one layer of a hyaluronic acid derivative.

Art Unit: 1651

Claims 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61, and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61, and 63 recite the phrase "as the inner matrix" in claim 1. There is insufficient antecedent basis for this limitation in the claims, because claim 1 is drawn to a multilayer composite material which is not preceded by a recitation of an inner matrix to which the phrase refers.

The claims are indefinite, because in claim 1 it is unclear how the elements of the claimed material are interrelated, resulting in multiple interpretations of the claimed invention structural cooperative relationship(s), though each combination defines a different structural cooperative associations and distinct inventions. The claims are indefinite because the identities and spatial and/or chemical associations of the component (multi)layers, matrices, composite material, and hyaluronic acid derivate(s) are unclear. The claims recite a multilayer composite material comprising: (a) a composite material in association with at least one layer; however, it is unclear if the "inner matrix..composite material" comprises components (i) and (ii) *with* the "at least one layer comprising a HA derivative" or if the "at least one layer" is a separate component (b) distinct from the matrix *or* if the HA derivative of the "at least one layer" is the same HA derivative of (i) or a separate entity. Also, the claim language is circular in that the composite material comprises a composite material and the matrix comprises, in part, a matrix. Furthermore, though the composition comprises a relative component, an "inner" matrix, but it is unclear as to what component(s) distinguish themselves as "outer" component(s) or references by which an inner component may be spatially compared. Since the claims are unclear, one

Art Unit: 1651

would not be apprised as to the metes and bounds of the claims, rendering the claims indefinite; however, this ground of rejection may be overcome, for example, by further separating the major components of the multilayer composite material and by distinguishing or associating terms which have multiple recitations in the claims, to the extent supported by the original disclosure.

In claim 14, the term “hydroxyapatite and/or tribasic calcium phosphate” is unclear because the terms are redundant by claiming alternate names of the single chemical species corresponding to the compound having the CAS# [12167-74-7] (see as evidence SIGMA-ALDRICH “Hydroxyapatite” Sigma-Aldrich Catalog <<http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIAL/289396>> accessed online 3/17/2008).

Claims 19 and 20 recite the term “the layers” of claim 1. The claims are indefinite, because the claims recite that the “multilayer” composite material has two or more layers *and* the component other than the inner matrix also has “at least one layer”. Thus, it is unclear if the term “layers” in claims 19 and 20 is further descriptive of either of the recited terms in claim 1 or if the term “layers” describes a third element of the composition. Each is a reasonable interpretation of the claims and each embraces different subject matter such that one would not be apprised as to what Applicant intends to embrace by the claims, thereby rendering the claims indefinite.

Additionally, the claims recite the phrase “wherein the layers are 2” and “wherein the layers are 3” which are relative terms requiring units of measure and/or an object against which the numerical terms “2” and “3” are referenced. Because the claims, as written, recite that the layers are a number *per se*, the claims are rendered indefinite. The phrases “layers are 2” or “layers are 3” are not defined by the claim and appear to be a literal translation of the foreign

Art Unit: 1651

language priority document, the specification does not provide a standard for ascertaining the requisite degree or “2” or “3”-ness, and one of ordinary skill in the art would not be reasonably apprised of the subject matter embraced by the claims, thus rendering the claims indefinite; however, this ground of rejection may be overcome by amending (e.g. to recite a multilayer composite material wherein the multilayer composite material comprises 2 layers (or 3 layers) *or* wherein the at least one layer comprises 2 layers (or 3 layers)) to the extent supported by the original disclosure.

The term "with a percentage" in claim 3 is a relative term which renders the claim indefinite, because the term lacks units (numerator/denominator compositions) against which percentage is referenced. The term "with a percentage" *per se* is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, rendering the claim indefinite.

In claim 33, reciting the term “2-dimensional structure” renders the claim indefinite, because all compositions in nature (including for example films), inherently have at least a degree of three measurable dimensions on the atomic-, molecular-, and/or bulk-scale; and thus it is unclear what compositions are embraced by 2-dimensional structures.

In claims 34, 37, 39, and 53 the abbreviations/terms HA, ACP, BMP, TGF, PDGF, FGF, EGF, IGF, and VEGF render the claims indefinite, because abbreviations may have multiple meanings and it is unclear from the claims what meaning(s) Applicant intends by the use of the abbreviations; however, this ground of rejection may be overcome, for example in the instance of

Art Unit: 1651

HA by reciting “hyaluronic acid (HA)” in the first recitation of the term in the claims (and in the specification) to the extent supported by the original disclosure.

In claim 16, the abbreviation of kD (or KD or kDa) correlated to molecular weight units appears to refer to the unit of kilodaltons; however, the variants kDs and KDs each used in the claims are unclear. To avoid potential confusion as to the meaning of the unit(s) or the identity of the “s” appended to the kD unit, a single variant of the abbreviation should be used consistently in the claims and without the “s” form(s) as the abbreviated unit of measure embraces the singular/plural form of the term which the unit describes.

Claim 36 contains the trademark/trade name ACP[®] (*c.f.* see Specification, page 10, indent (5)). Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a critical component of the composition and, accordingly, the identification/description is indefinite. Furthermore, the parenthetical recitation of the trademarked composition is unclear as to whether the preceding text is a generic description of the trademarked composition, is an exemplary species, or describes a separate element of the composition. The use of the trademarks has been noted in this application; and, to the extent that a tradename is used in a claim, it should be capitalized and include the appropriate

Art Unit: 1651

trademark symbol wherever it appears (*e.g.* ACP[®]) and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks (see MPEP 608.01(v)).

Claim Rejections - 35 USC § 103

Claims 1-17, 19-34, 37, 39, 42-53, 61, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over VALENTINI (US 5,939,323).

The claims are generally drawn to a multilayer composition comprising an inner matrix of a hyaluronic acid (HA) derivative and a matrix in association with a hyaluronic acid derivative. The elected species are further drawn to an HA benzyl ester and tribasic potassium phosphate (CAS# [12167-74-7], hydroxyapatite).

VALENTINI teaches a composition comprising hyaluronic acid (HA) and derivatizing HA, including esterification of HA with uncharged organic groups, including benzyl groups, to decrease water solubility of the material. Valentini also beneficially teaches varying the degree of substitution on the hyaluronic acid backbone, including 100% esterification with benzyl-derivatized HA (*e.g.* column 1, ¶4; columns 4 and 5). Valentini further teaches that the scaffold-forming composition may be further modified by combining the HA with a second phase, including hydroxyapatite or tricalcium phosphate (column 3, ¶3) and further including coating the composition with a second polymer (column 10, indent (2)(f)). Valentini additionally teaches that the composition is provided in a three-dimensional biodegradable scaffold comprised of liner HA molecules (column 1, ¶4 and structure), which can be fabricated or trimmed into any

Art Unit: 1651

size *and* shape *and* any pore size (column 2, ¶1; column 9, ¶2 and 6; column 13 line 1-3), including contacting with water/solvent.

A chemical is inseparable from its properties. Since the components taught by the prior art are disclosed by Valentini to function for the same purpose and to the extent as is instantly claimed/disclosed (i.e. as bone repair/substitute compositions); thus, absent a definition of the minimum structural requirements defining the arrangement of compositions into species of forms including a sponge, (non)woven tissue, paste, granule, powder, etc. *and* absent objective evidence as to the criticality of the particular arrangement(s) of the composition components upon the functioning of the compositions to the extent claimed/disclosed, the compositions are deemed to still be obvious in view of the prior art compositions. As such, one may broadly and reasonably interpret the forms as compositions varying merely in linear dimensions and/or states of hydration and thus corresponding to the compositions made obvious by Valentini, and thus Valentini constitutes a teaching that the claimed forms are within the purview of one of skill and thus would have been prima facie obvious to provide the composition in the form to the extent claimed for the same recited intended use(s).

It would have been obvious to vary the form of the composition, the percentage of derivatization in the HA derivative (i.e. varying the proportion of materials in the esterification of HA) because Valentini teaches that the composition may be trimmed and manipulated to attain the desired porous composition of the desired dimension and of any dimension (*any* size and shape). Valentini is relied upon for the reasons discussed above. If not expressly taught by Valentini, based upon the overall beneficial teaching provided by this reference with respect to the selection of and trimming to size of the composition in the manner disclosed therein, the

Art Unit: 1651

adjustments of particular conventional working conditions (e.g., determining the ratio of components, determining one or more suitable size ranges in which to provide a composition, determining the drying time or contact time with solvent(s)), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Furthermore, it would have been obvious to further incorporate bioactive compounds into the composition, because Valentini beneficially teaches bioactive agents which are useful in the invention, including antibiotics, cytokines, molecules that effect cell migration, and bone morphogenic protein, among other compounds (Column 6, ¶1). One would have been motivated to incorporate said agents, because Valentini teaches that the agents are useful in the composition to promote ingrowth of the cells into the implantable material. One would have had a reasonable expectation of success in making a bioactive agent-supplemented composition, because the success of the composition depends merely upon the *contacting* of the primary HA composition scaffold with the agent and since the contacting may occur with the HA and the agent before or after scaffold formation and either within or upon the composition non-covalently or covalently (column 6, ¶4).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Art Unit: 1651

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of objective evidence to the criticality of some undisclosed feature, side-by-side comparison(s), or objective evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aaron J. Kosar whose telephone number is (571) 270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Aaron Kosar
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner. Art Unit 1651